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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/844,336	04/18/1997	PAMELA R. CONTAG	8678-004-999	7227

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ROBINS & PASTERNAK LLP
1731 EMBARCADERO ROAD
SUITE 230
PALO ALTO, CA 94303

EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/844,336	CONTAG ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,21,22 and 25-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,21,22 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the Appeal Brief filed on 8-24-2010, PROSECUTION IS HEREBY REOPENED. New grounds of rejection set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Claims 1, 5-6, 21-22 and 25-27 are pending and currently under examination.

New Grounds of Objection

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, on which said claims depend, limits the intracellular

enzymatic signal transforming domain to being either a phosphorylase or a phosphatase. PhoQ is a kinase.

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, on which said claims depend, limits the intracellular enzymatic signal transforming domain to being either a phosphorylase or a phosphatase. PhoQ is a kinase.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3-6, 9, 21-22 and 25-27 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues:

1. The instant claims do not encompass limitless combinations of transmembrane fusion proteins as they require that the extracellular domain be an antibody and the intracellular domain be a phosphorylase or phosphatase (as exemplified with PhoQ).

2. The claimed biodetectors make use of known signal transduction cascades.

3. Transmembrane fusions of antibodies and phosphatases or phosphorylases were well known in the art and described in the instant specification (i.e. Example 2).

4. The chemical structures of light generating proteins are clearly described in the instant specification.

5. The Capon decision is applicable to the case on appeal since the components of the claimed biodetector were will known in the art.

6. The Examiner has improperly based the written description rejection on the grounds that embodiments must be empirically determined. The written description requirement does not require that Applicant list all possible embodiments.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1, 2 and 4, while the components of the instant invention may have been known in the art, the compatibility of said components which would give rise to a functional biodetector was not. The instant claims encompass biodetectors comprising limitless combinations of transmembrane fusion proteins (comprising an extracellular ligand binding domain [i.e. antibody] and a membrane intracellular enzymatic signal domain [i.e. a phosphatase or phosphorylase], transducers and a responsive element which generates a detectable light signal). The claimed biodetectors are composed of components that can be either prokaryotic or eukaryotic in nature. Consequently, the

instant claims encompass the mixing and matching of thousands of different prokaryotic and eukaryotic elements that must work together to form a functional biodetector. The single functional embodiment (the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element) utilizes bacterial elements and promoters in a bacterial biosensor. The instant claims, on the other hand, encompass the mixing and matching of prokaryotic and eukaryotic elements of in a fashion unique to the art. Said art is silent with regard to efficacy of using eukaryotic elements within a bacterial biosensor or vise versa. Moreover, a survey of the relevant art demonstrates an inability to introduce a complete eukaryotic signal transduction system in any bacterial cell which allows for functionality. While the specification discloses a functional antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element, said biodetector is not encompassed by the instant claims as the PhoQ system is a kinase and the instant claims are limited to phosphatase and phosphorylase based biodetectors (see Walsh, Enzymatic Reaction Mechanisms, W.H. Freeman and Company, 1979 page 185). The specification is silent to what specific combinations elements will work. On the contrary, the specification discloses that one has to screen for operative and inoperative embodiments at each level and provides no guidance as to what specific phosphatases and phosphorylases would be functional in a given biodetector (see pages 26-28 of the specification). Consequently, the specification does not disclose any correlation between structure (i.e. the components of the biodetector) and function (the ability to function as a biodetector) as required by the written description requirement. Given the lack of guidance within the specification, the skilled artisan would not know what **combination of elements** would produce a biodetector that functions as claimed. Applicant is reminded that adequate written description requires more than a mere statement that it is part of the invention and *reference to a potential method for isolating it*. The functional fusion protein itself is

required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

With regard to Point 5, the biotechnology art as it relies to biodetectors not considered a "mature technology". Moreover, the crux of the *Capon* decision is what is known in the art. In the *Capon* decision, the CAFC stated "In summary, the Board erred in ruling that §112 imposes a *per se* rule requiring recitation in the specification of the nucleotide of claimed DNA when that sequence is already known in the field. However, the Board did not explore the support for each of the claims of both parties in view of the specific examples and general teachings in the specifications and the known science with application of precedent guiding review of the scope of the claims." The CAFC determined that the correlation between structure and function, required to meet the written description requirements, were known in the art. This is not the case with regard to the instant claims as the specifics components of the claimed biodetector that would give rise to a functional biodetector are not known in the art. Consequently, the *Capon* decision is not germane to the instant rejection.

With regard to Point 3, a survey of the art demonstrates that Applicant's assertion that transmembrane fusions of antibodies and phosphatases or phosphorylases were well known in the art.

With regard to Point 6, contrary to Applicant's assertion, the instant rejection is based on the specification not disclosing any correlation between structure (i.e. the components of the biodetector) and function (the ability to function as a biodetector) as required by the written description requirement.

As outlined previously, the instant claims are drawn to a biodetector comprising a transmembrane fusion protein comprising an extracellular ligand-specific moiety comprising an antibody and a membrane intracellular enzymatic signal-transforming domain (i.e. signal-converting element {phosphatase or phosphorylase); a transducer and a responsive element (transcription activation element) coupled to a reporter gene (luciferase) via said responsive element. Said biodetector may further comprise a bacterial cell.

The specification discloses a biodetector comprising a fusion protein consisting of an antibody heavy chain and an active domain of PhoQ, PhoP (signal transducer) and the *lux* operon coupled to the Pho promoter. This biodetector meets the written description provision of 35 USC 112, first paragraph. However, the aforementioned claims are directed to encompass biodetectors comprising limitless combinations of transmembrane fusion proteins (comprising an extracellular antibody domain and an intracellular enzymatic signal domain), transducers and reporter genes/operons. None of these biodetectors meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. The transmembrane fusion protein of the claimed biodetector must be able to activate a given transducer via its intracellular enzymatic signal transforming domain upon the binding of the "ligand" to the extracellular antibody. The transducers must be able to trigger either directly or indirectly, the activation of a transcription activating element (promoter) to effect the activation of the responsive element (reporter gene or operon). The Specification discloses that said transducer may be any molecule that can recognize and respond to a change in conformation, electrical charge, addition or subtraction of any chemical subgroup and is capable of triggering a detectable response (see page 16 of the specification). With the exception of the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled

to the *lux* operon as its responsive element, the specification is silent with regard to what specific combinations of transmembrane proteins, transducers and responsive elements would result in a functional biodetector.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the aforementioned antibody/PhoQ based biodetector, the skilled artisan cannot envision the detailed chemical structure of the encompassed biodetectors, regardless of the complexity or simplicity of the method of screening for active components (isolation). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:
...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli ,* 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.

The claimed biodetectors are unrelated by structure, the genus of components making up said biodetectors is vast; there is no description of any structure that meets the limitation. Mere function does not describe a structure, because the specification does not provide relevant identifying characteristics, including functional characteristics when coupled with known or disclosed correlation between function and structure. The courts have held that in these instances, the specification lacks written description see *Enzo Biochem Inc. v. Gen-Probe Inc.* 63 USPQ2D 1609 (CAFC 2002) and *University of Rochester v. G.D. Searle & Co.* 69 USPQ2D 1886 (CAFC 2004). When the genus is vast and compounds are claimed by function alone and the specification lacks a known or disclosed correlation between structure and function, the written description of the specification does not convey possession of the claimed genus. Additionally, possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Therefore, only aforementioned antibody/PhoQ based biodetector, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed is not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

New Grounds of Rejection

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 recites the limitation "wherein said intracellular enzymatic signal transforming domain is a PhoQ intracellular enzymatic domain" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim 25 recites the limitation "wherein said intracellular enzymatic signal transforming domain comprises an active domain of PhoQ." in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claims 21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Said claims are rendered vague and indefinite by the use of the term "PhoQ" in reference to the intracellular enzymatic signal transforming domain. Claim 1, on which said claims depend, limits the intracellular enzymatic signal transforming domain to being either a phosphorylase or a phosphatase. PhoQ is a kinase. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Patricia Duffy can be reached on (571) 272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Patricia A. Duffy/
Acting Supervisory Patent Examiner, Art Unit 1645

/Robert A. Zeman/
Primary Examiner, Art Unit 1645
November 3, 2010